Remarks

Amendments to the Claims

Claim 5 is amended to correct an obvious clerical error. The amendment does not add new matter.

Rejection Under 35 U.S.C. § 102(e)

Claims 1, 2, 4, 5, 7, 8, and 13-21 stand rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,995,299 (Wu). Applicants respectfully traverse the rejection. Wu is not prior art to the present application.

Wu was filed August 15, 2001 as a continuation-in-part of PCT/US00/05713 which itself is a continuation-in-part of Serial No. 09/431,901 filed on November 2, 1999 (now U.S. Patent 6,525,242). Applicants note that the '242 patent was not used to reject the present claims. However, even if the cited Wu patent were entitled to its earliest claimed priority date, Applicants can swear behind the November 2, 1999 filing date of Serial No. 09/431,901.

A Declaration of Dr. William Beschorner under 37 C.F.R. § 1.131 accompanies this paper.[1] The Declaration establishes that the Applicants conceived of the claimed method before November 2, 1999 and diligently worked to reduce it to practice at least until provisional application Serial No. 60/411,790 was filed on September 19, 2002.

Serial No. 60/411,790, to which the present application claims benefit, describes and enables the method of claims 1, 2, 5, 7, 8, and 13-21. Paragraph 17 generally discloses the methods of claims 1 and 18:

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[1] Of the three named inventors only Dr. Beschorner made and signed the Declaration. Dr. Beschorner is an applicant under 37 C.F.R. § 1.47(a); see Declaration ¶ 1.

> One embodiment of the invention provides methods for enhanced growth of foreign cells within non-human mammals. The methods employ conditional and controlled reduction of select cells within a tissue of a fetal non-human mammal, followed by regeneration of the tissue with the foreign cells. The destruction of the fetal cells does not affect the corresponding cells in the maternal host or the foreign regenerating cells. The destruction of fetal cells is specific for the cells that are being replaced during tissue regeneration.

In paragraph 51, Serial No. 60/411,790 discloses expression of a suicide gene product in native cells, as recited in claims 2 3, 20, and 22:

> Preferably the fetus is a chimeric animal with one transgenic and one normal parent. Typically, the male parent is a transgenic animal that expresses a suicide gene. A "suicide gene" is a gene that encodes an enzyme that converts a nontoxic prodrug into an active toxin that causes apoptosis. The suicide gene is typically viral or prokaryotic. Examples of suitable suicide genes include, but are not limited to, thymidine kinase (either wild-type or comprising a mutation), cytosine deaminase, carboxylesterase, carboxypeptidase, deoxycytidine kinase, nitroreductase, guanosine xanthin phosphoribosyltransferase, purine nucleoside phosphorylase, and thymidine phosphorylase. In the absence of the prodrug, expression of the suicide gene preferably has no toxic or other adverse effects on normal cellular metabolism.

The tissue types recited in claims 4, 13, and 21 are described in paragraph 27:

> One or more tissues in the fetal host is injured and partially or completely eliminated, making the tissue receptive to regeneration with foreign cells. Cells of most tissues can be regenerated using methods of the present invention. A "tissue" comprises a group of similarly specialized cells that perform a common function (e.g., liver, hematopoietic, endothelial, neural, epithelial, retinal, pigment epithelial, myocardial, skeletal muscle, smooth muscle, lung, intestine, kidney, endocrine, cartilage, or bone cells).

Serial No. 60/411,790 discloses the fetal non-human mammals listed in claim 5 at paragraph 41: "Fetal and maternal host animals preferably are non-human mammals, such as non-human primates, artiodactyls, carnivores, rodents, or lagomorphs. Large mammals, such as pigs, sheep, cows, or non-human primates, are useful for producing organs or large numbers of

cells suitable for human transplantation." This paragraph also supports claims 14 and 15, which recites using artiodactyls and pigs, a species of artiodactyl, respectively.

Claim 16 recites that the artiodactyl is transgenic. Paragraph 48 discloses using transgenic pigs: "For example, to grow human liver cells (hepatocytes) in pig livers, a non-transgenic female pig (gilt or sow) would be bred with a transgenic male pig (boar) [having] a suicide gene controlled by a liver specific promoter such as an albumin or an α-fetoprotein promoter."

The foreign replacement cells can be from the same species as the host (claim 6) or a different species (claim 7). Paragraph 72 discloses both: "The cells may be from the same species or from a different species (xenogeneic) and may be primary cells or cells of a cell line." The method of claim 8 uses human cells, which is disclosed at paragraph 77: "For example, human cells capable of regenerating the liver, such as hepatocytes, liver progenitor cells, or hematopoietic stem cells, can be injected into fetal pigs."

Paragraph 62 discloses use of liposomes to destroy cells (claim 9) and use of tissue-specific targeting ligands (claim 11), such as antibodies (claim 12):

> Specificity for the target tissue is determined by the ligand or antibody on the surface. The specific antibody or ligand would be determined by the system used. For example, to deplete fetal hepatocytes, liposomes would be produced carrying a ligand for the asialoglycoprotein receptor expressed on hepatocytes.

Use of liposomes to deliver a toxin or a prodrug, as recited in claim 10, is disclosed in paragraph 64: "The appropriate prodrug can be contained within the liposomes or immunoliposome or can be administered separately."

Claims 17 and 19 recite a method where the maternal cells are not transgenic. Paragraph 46 discloses using non-transgenic sows: "In one embodiment, a non-transgenic female mammal

is bred with a transgenic male mammal containing a suicide transgene whose expression is controlled by a tissue-specific promoter."

Serial No. 60/411,790 describes and enables each aspect of the claimed methods and is therefore a constructive reduction to practice of the claimed invention.

Dr. Beschorner's Declaration establishes that Wu is not prior art to the present application. Please withdraw the rejection.

Rejections Under 35 U.S.C. § 103(a)

The Office Action maintains the rejection of claims 1 and 3 as obvious over Wu in view of Loeb (U.S. Patent 6,451,571) and the rejection of claims 1 and 9-22 as obvious over Wu in view of Sorscher (U.S. Patent 6,017,896). Applicants respectfully traverse both rejections.

As noted above, Wu is not prior art to the claimed subject matter. Loeb and Sorscher, even if combined, do not teach or suggest the subject matter of independent claim 1 and dependent claims 3 and 9-22.

Please withdraw the rejections.

Respectfully submitted,

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